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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/072,320 | 02/07/2002 | Russell Mumper | NANO:002USD1 | 5127 |

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| EXAMINER | |
|---|---|
| BERKO, RETFORD O | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1615 | |

DATE MAILED: 11/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/072,320 | MUMPER ET AL. | |
| | Examiner | Art Unit | |
| | Retford Berko | 1615 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *30 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *33-47,51 and 56-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-47,51 and 56-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## *DETAILED ACTION*

**Acknowledgement**: Receipt of Amendment filed April 30, 2004 is acknowledged.

### Status of Claims

1. Claims pending following applicant's amendment are: claims 33-47, 51 and 56-58.

2. Claims 1-32, 48-50, 52-55 and 59-62 are withdrawn or cancelled in view of the amendment.

### Restriction/Election

Reference is made of the Restriction and election previously executed for the record.

This application contains claims directed to the following patentably distinct species of the claimed invention:

a) "the wax-film composite of claim 33, wherein the molecule of interest is amlexanox"

b) "the wax-film composite of claim 33, wherein the molecule of interest is triclosan"

c) "the wax-film composite of claim 33, wherein the molecule of interest is lodocaine, benzocaine, or dyclonine"

d) "the wax-film composite of claim 33, wherein the molecule of interest is a peptide or protein"

(e) the wax-film composite of claim 33, wherein the molecule of interest is at least one benzodiazepine drug or derivative thereof"

(f) "the wax-film composite of claim 33, wherein the molecule of interest is hirudin or hirudin complexed with a substance of opposite charge"

(g)"the wax-film composite of claim 53, wherein said substance of opposite charge is chitosan or protamine"

(h) "the wax-film composite of claim 33, wherein the molecule of interest is plasmid DNA or plasmid DNA complexed with a substance of opposite charge such as chitosan, protamine, or a cationic lipid".

In a telephone conversation, applicant was requested, as mandated by 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, a claim for a "wax-film composite" is generic.

During the telephone conversation with Attorney Michael C. Barrett on January 5, 2004, applicant elected without traverse prosecution for claim 51--reciting "the wax-film composite of claim 33, wherein the molecule of interest is a protein or peptide".

Therefore, claims 48, 49, 50; and claims 52, 53, 54, 55, 59, 60, 61 and 62 are withdrawn from consideration in this office action.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

**Withdrawal of Claim Rejections**

1. The rejections of claims 35, 36, 46, 47, 51, 56, 57 and 58 under 35 USC Sec. 112, second paragraph, as being indefinite have been withdrawn in view of applicant's arguments and amendment to the claims.

2. The claim rejections under 35 USC Sec 103 as being unpatentable over Eckenhoff et al (US 4, 959, 218) in view of over Biegajski et al (US 5, 700, 478) are maintained in view of the reasons set forth below.

**Claim Rejections - 35 USC § 103**

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 33-47, 52, and 56-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eckenhoff et al (US 4, 959, 218) over Biegajski et al (US 5, 700, 478).

According to applicant, claims 33-47 are directed toward a wax-film composite comprised of pH-sensitive mucoadhesive, film-forming layer and a water-insoluble wax layer, with known concentrations (10-80%); the water-insoluble swellable adhesive polymer is polyacrylic acid or a copolymer of methacrylic acid and acrylic or methacylic ester (Noveon, Carbomer or Eudragit). The pharmaceutical wax used is for forming the insoluble wax layer can be beeswax, emulsifying wax or microcrystalline wax.

The claims are further directed towardthe active pharmaceutical compounds in the wax-film composite—antimicrobial or diagnostic agent, amlexanox, lidocaine, peptide or

benzodiazepine drug and the wax film composite is applicable to the delivery of such active agent to the skin, mouth, nasal cavity or other mucosal surfaces.

It is generally known in the art that several bioadhesive, and specifically mucoadhesive, (CMC), hydroxypropymethylcellulose (HPMC), polyacrylic acid and their derivatives, pectin, alginic acid, chitosan, polyvinylpyrrolidone, hyaluronic acid and polyvinylalcohol. It is also generally known in the art that the most frequently used mucoadhesive polymer is Carbopol (Carbomer), which is a high molecular weight polyacrylic acid polymer.

Eckenhoff et al (Patent (218) disclose a drug delivery device adapted to take several forms, shapes and forms for delivering medicaments to subcutaneous spaces in an animal or human, e.g. buccal, cervical, oral sites (col 7, lin 15-25). The material used for the delivery device in Patent '2 1 8 is Carbopol (Carbomer) or other water swellable polymers (col 1 1, lin 25-60) having functional g'roups such as hydroxyl or carboxyl groups (col 7, lin 50-60 and col 8, lin 40) as well as polyelectrolyte complexes (col 1 1, lin 40- 4sl---these functional groups and complexes render the polymer layers pH-sensitive. Significantly, Patent '218 also discloses the use of wax layer formed of microcystalline wax (col 15, lin 1-15) and that the disclosed wax-film composite has at least one medicament, e.g. anti-inflammatory compound, protein drug, peptides (col 10, lin 30-45).

Patent '218 does not specifically teach the use of terms pH-sensitive, mucoadhesive; does not teach Eudragit or wt% or amounts of the ingredient polymers, and other physical parameters such as melting point of wax, the thickness of the wax-film and the release time for the delivery device to deliver the active compound to the site of application in the body.

Biegajski et al (Patent '478) discloses double layered, mucoadhesive drug delivery device wherein the adhesive layer and the second polymer layer contain the drug to be delivered (abstract, col 35 lin 30). Patent '478 is suggestive that a wax can be used as suitable layer (col 4, lin 35). Patent '478 teaches the use of Eudragit polymethacrylate copolymers (col 22, lin 15) and Carbopol 934 (col 28, lin 40-45) for making the adhesive layer for the drug delivery device and the wt% of polymer components (col 8, lin 50). Patent '478 discloses wax-film composite wherein the mucoadhesive layer is a copolymer of methacrylic acid esters with diethylaminoethyl methacrylate (col 33, lin 55-60). Patent '478 discloses the melting temperature of the wax (col 9, lin 10; col 10, lin 55 and col 34, lin 35), the use of polyvinyl pyrrolidone or polyvinyl alcohol polymer (col 28, lin 40). Patent '478 teaches that adherence of the wax-film composite to the mucosal site lasts beyond one hour (col 5, lin 25 and col 6, lin 30).

One of ordinary skill would have been motivated to make mucoadhesive drug delivery device using polyacrylic acid cross-linked with polyalkenyl ether or divinyl glycol as the material for making the wax-film composite, giving wt% or amounts of the ingredient polymers, physical parameters such as melting point of wax, the thickness of the wax-film and the release time for the delivery device to deliver the active substance in a time more than 1 hr as claimed by applicant. One of ordinary skill would have expected to obtain effective drug delivery of beneficial agents through the subcutaneous space over time using the method in the prior art because Patent '478 suggests the use of wax film for constructing the drug delivery device (col 4, lin 35-45 and col 5, lin 20-30). Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time it was made.

**Response To Arguments**

Applicant's arguments have been considered but are found unpersuasive:

Applicant argues that Patent 4,959,218 i.e. the Eckenhoff et al. reference does not disclose or suggest explicit elements required by claim 33 and that the basic criteria needed for establishing a prima facie case for obviousness have not been met in that there is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings with another reference and that there is no reasonable expectation of success in combining the references cited. Applicant contends that a wax-film composite comprised of a pH-sensitive mucoadhesive layer and a water-insoluble wax layer is not taught or suggested by the references either alone or in combination.

In response, as discussed, Patent '218 discloses the use of wax layer for making a drug delivery device, the wax-film layer formed is made of microcystalline wax (col 15, lin 1-15 and lin 45-55) and that the disclosed wax-film composite at least has one medicament, e.g. anti-inflammatory compound, protein drug, peptides (col 10, lin 30-45). The motivation to combine is provided by the suggestion by the disclosure in Biegajski et al (Patent '487), suggesting or by implication disclosing that the use of wax layer that is a mucoadhesive delivery device is beneficial in so far as there is extended or delayed onset of release of drug across the membrane to mucosal surface (col 4, lin 21-45).

Applicant argues that the laminate device disclosed in the Biegajski reference (Patent '478) teaches that the mucoadhesive layer be fully comprised of water-soluble components, that all layers of the laminate devices of the invention are water-soluble, and they therefore dissolve

or disperse entirely in the fluids secreted within the body cavity. Applicant contends that the inclusion of an additive such as a wax to a polymer layer does not make the layer a wax-layer.

In response, the Biegajski et al (Patent '478) is relied upon for its disclosure of forming drug delivery devices made of double layered, mucoadhesive polymers and the suggestion that wax can be incorporated within the occlusive polymers in such composites with advantages as previously mentioned. This becomes significant and important basis for establishing the prima facie case for obviousness because when the disclosure is combined with the detaching in Eckenhoff et al (Patent '218), wherein drug delivery devices are formed using wax layer, (col 15, lin 1-15 and lin 45-55), one of ordinary skill in the art can expect reasonable level of success in making a drug delivery device made of polymers as disclosed in the two references.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

**Correspondence**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Retford Berko** whose telephone number is 571-272-0590. The examiner can normally be reached on M-F from 8.00 am to 5.30 pm

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Thurman K Page**, can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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